

REMARKS/ARGUMENTS

Claims 26-28, 41-43, and 51-53 are presently pending, and will remain pending upon entry of the instant response to the record. In particular, Applicants have provided the additional references/support as agreed upon with the Examiners, establishing the suitability of a comparative example in ZD1611, Example 64 of Bradbury, et al. Such agreement was reached as described below solely in order to expedite prosecution of the instant application. *No new matter has been added.*

As a preliminary matter, Applicants would like to thank Examiner Marschel and Examiner Royds for their willingness to reconsider the present application in light of the Examiner Interviews generously granted to Applicants' attorney.

Moreover, amendment and/or cancellation of the claims during pendency of the application are not to be construed as acquiescence to any of the objections/rejections set forth in any Office Action, and were done solely to expedite prosecution of the application. Applicants submit that claims were not added or amended during prosecution of the instant application for reasons related to patentability. Applicants reserve the right to pursue the claims as originally filed, subsequently amended or added, or similar claims, in this or one or more subsequent applications.

Claim Rejections under 35 USC §103

Rejection of Claims 26-28, 41-43, and 51-53 under 35 USC §103(a)

Claims 26-28, and 41-43, as well as newly added claims 51-53, remain rejected under 35 USC §103(a) as being unpatentable over Bradbury et al. in view of Hsu et al. and Nelson et al. Applicants have respectfully traversed this rejection and maintain this traverse herein.

In order to provide additional clarity, Applicants were granted a telephonic interview with Examiner Marschel on March 30, 2010, a summary of which is provided below as requested by the Examiner. Applicants first presented arguments related to the prima facie case for obviousness, arguing the lack of motivation to combine the references based on a central reference of Bradbury et al., and highlighted that Bradbury et al. would not have been arrived upon as the central reference without hindsight reconstruction. Applicants further suggested that even if a prima facie case for obviousness were established, secondary considerations would support non-obviousness. In this regard, Applicants noted that it had been previously argued

that the specification (including examples) asserted unexpected and surprising results; and Applicants further offered a comparison between Compound I and a competitor ET-1 antagonist, Atrasentan (wherein such data had been provided by means of a post-filing date reference related thereto). In response, Examiner Marschel indicated that he and Examiner Royds would reconsider the pending claims in light of the arguments presented in the interview.

A telephone message received from Examiner Marschel on April 1, 2010, provided a synopsis of the results of the reconsideration. While no comment was made as to the arguments addressing the prima facie case, Examiner Marschel indicated that if secondary considerations were to be relied upon in the form of unexpected results then Applicants would need to provide comparative data to between Compound I (ZD4045, Example 36 of Bradbury et al) and the "closest prior art" indicating that Compound I would have been unexpected with respect to this "closest prior art."

Applicants, very much appreciative of the time afforded for the reconsideration, requested an additional discretionary telephonic interview seeking clarity as to the identity of the "closest prior art" reference; and further which example/species/compound within this reference would be suitable to compare to Compound I. In the generously granted telephonic interview with Examiner Marschel and Examiner Royds on April 8, 2010, Applicants inquired as to what the examiners considered as the closest prior art. Examiner Royds suggested that the closest prior art was Bradbury et al., in that Bradbury had been identified by a structure search of Compound I. Applicants suggested that it was the very manner of selection of this reference, based upon the presence of Compound I, which made it very difficult to choose a comparison compound within this reference, as the closest and seemingly only relevant prior art compound in Bradbury was the compound itself.

However, in order to expedite prosecution, Applicants inquired as to whether *any* of the compounds in the application would be allowable for the requested comparison; and if so, would comparison to Example 64 be sufficient. Applicants explained that this compound, ZD1611, was "well-publicized" at the time of the filing of the instant application as the other front runner in the AstraZeneca (then known as Zeneca) cardiovascular program along with ZD4054, Example 36 of Bradbury. Applicants suggested that the ordinarily skilled artisan who was aware of ZD4054 in Bradbury, would certainly have been aware of ZD1611 in a similar fashion. The Examiners then agreed that a sufficient showing of a number of references that supported this "well-publicized" nature would support the use of Example 64, ZD1611, as a comparative example for

demonstrating the secondary considerations of unexpected results. Accordingly, Applicants have provided herewith ten references that highlight the well-publicized nature of ZD1611 and were available prior to the filing of the instant application; including one [WILSON et al. Pharmacological profile of ZD1611, a novel, orally active endothelin ET_A receptor antagonist. J Pharmacol Exp Ther, 1999, 1085-1091, 290(3)] that provides the comparative data requested by the Examiner. The following is an excerpt from the ABSTRACT of this reference, with the requested comparison information:

ZD1611 competitively inhibits ¹²⁵I-labeled ET-1 binding at human cloned ET_A and ET_B receptors with pIC₅₀ values of 8.6 ± 0.1 and 5.6 ± 0.1 , respectively, showing 1000-fold selectivity for the ET_A receptor.

Applicants reiterate that the instantly claimed invention shows no measurable ET_B activity, yet Example 64 of Bradbury, ZD1611, to which the ordinarily skilled artisan would have been motivated to examine (as supported by the ten references provided herewith) shows a measurable ET_B pIC₅₀ of 5.6 ± 0.1 , in contrast to the claimed invention. Such a showing clearly supports the position of unexpected results for the claimed invention, and should be sufficient to rebut any prima facie arguments of obviousness.

Moreover, Examiner Royds and Examiner Marschel graciously agreed to consider this showing prior to the end of the statutory period; and that such a showing, in principle should be sufficient to address the present rejection of the claims under 35 USC §103.

For completeness of the record, Applicants also addressed the prima facie case for obviousness in the second telephonic interview of April 8, 2010, by suggesting that while understandable to conduct a search using Compound I to arrive at Bradbury et al, this motivation alone would not be sufficient to identify Bradbury as the primary reference. Examiner Royds indicated that she believed this was a proper selection. While Applicants respectfully disagreed, in order to expedite prosecution Applicants were willing to move forward and address the support for secondary considerations that was expected to resolve the rejection under §103.

Accordingly, Applicants respectfully request withdrawal of the rejection of claims 26-28, 41-43, and 51-53 under 35 USC §103(a), and favorable reconsideration.

Claim Rejections under Obviousness-Type Double Patenting

Rejection of Claims 26-28, 41-43 and 51-53 under Obviousness-Type Double Patenting

Claims 26-28, 31-32 and 41-43 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 42-44 of co-pending U.S. Application No. 11/720,001 in view of Bradbury et al. (U.S. Patent No. 5,866,568; 1999), Hsu et al., and Nelson et al. Applicants incorporate by reference the arguments related to 35 USC §103(a) above and request withdrawal of the rejection of claims 26-28, 31-32 and 41-43 on the ground of nonstatutory obviousness-type double patenting.

Rejection of Claims 26-28, 41-43, and 51-53 under Obviousness-Type Double Patenting

Claims 26-28, 41-43, and 51-53 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 42-44 of co-pending U.S. Application No. 12/483,821 in view of Bradbury et al, Hsu et al., and Nelson et al. Applicants incorporate by reference the arguments related to 35 USC §103(a) above and request withdrawal of the rejection of claims 26-28, 41-43, and 51-53 on the ground of nonstatutory obviousness-type double patenting.

Request for Phone Interview

Once the Examiner has had an opportunity to review the comments made herein, Applicants respectfully request a phone interview with the Examiner in order to discuss any final details that may help result in an allowance of the application with all pending claims.

CONCLUSION

Applicants respectfully request favorable reconsideration of all rejections/objections. As noted above, if a telephone conversation with Applicants' attorney would help to expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' attorney at the telephone number below.

The above amendments have been made without prejudice to Applicants right to prosecute any cancelled subject matter in a timely filed continuation application.

A petition for a three month extension of time is being filed herewith, the Commissioner is hereby authorized to charge any deficiency in the fees or credit any overpayment to deposit account No. 50-3231, referencing Attorney Docket No. 100815-1P US.

Respectfully submitted,

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